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TITLE: Positioning Vascularized Composite Allotransplantation within the Spectrum of Solid Organ Transplantation

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14. ABSTRACT The purpose of this project is to enable more patients to access VCA transplantation. The work in Louisville will focus on using non-invasive imaging techniques that can be used to monitor vessels and nerves in VCA recipients (Aim 6). The goal is to identify changes while there is still time to intervene. Studies are initiated using infrared imaging of ICG dye to study blood perfusion and lymphatic drainage in our hand transplant patients. We are extending our studies of vessel wall thickness using very high resolution ultrasound, and including non-invasive studies of nerve anatomy. In Aim 7 we established a rodent model to study VCA vasculopathy, both with respect to imaging modalities and what factors initiate or exacerbate graft vasculopathy. Initial IR-ICG imaging studies of graft perfusion correlate well with acute graft rejection in our animals. Finally in Aim 8 we will develop standardization of protocols and clinical monitoring and treatment for VCA targeting vascular health. We propose to serve as the central site for the standardization of bioimaging assessment of vasculopathies in hand and face allotransplants. The ultimate goal is to expand the available options for individuals with combat-related injuries in need of complex tissue reconstruction by elevating VCA to the level of an established therapy for use in appropriately selected personnel with severe traumatic tissue loss.					
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INTRODUCTION: The principal objective of this project is to hone vascularized composite allotransplantation (VCA) into a useful therapeutic option for patients in need of advanced tissue reconstruction and replacement. This is a multi-institutional and multi-disciplinary project between the Louisville VCA Program, which is composed of four different institutions in Louisville, the University of Pennsylvania, the University of Maryland, and at this point, Duke University. The work in Louisville is focused on aims 6,7 and 8 of the Statement of work. Specifically in Aim 6 we will evaluate less invasive bio-imaging modalities with standard of care biopsy and peripheral blood analysis to assess vasculopathies associated with VCA in patients. In Aim 7 we will establish disease mechanisms associated with vasculopathy in pre-clinical models of VCA. Finally in Aim 8 we will develop standardization of protocols and clinical monitoring and treatment for VCA targeting vascular health. We propose to serve as the central site for the standardization of bioimaging assessment of vasculopathies in hand and face allotransplants. The ultimate goal is to expand the available options for individuals with combat-related injuries in need of complex tissue reconstruction by elevating VCA to the level of an established therapy for use in appropriately selected personnel with severe traumatic tissue loss.

KEYWORDS: VCA, vasculopathy, animal model, high resolution ultrasound, Fluorescence angiography, immune monitoring, graft rejection, histology, standardization, hand transplant, face transplant

ACCOMPLISHMENTS:

The major goals of this project are focused on Aim 6, 7 and 8 of the Statement of work, which are as follows:

Aim 6. To evaluate less invasive bio-imaging modalities with standard of care biopsy and peripheral blood analysis to assess vasculopathies associated with VCA in patients.

Hypothesis: Vascular events associated with VCA can be identified and the therapeutic intervention efficacy can be assessed using minimally invasive, bioactive contrast imaging of the transplant vasculature. To test the hypothesis, we will perform vascular

assessments in existing and new VCA patients in the Consortium using our bioimaging modalities. Image findings will be correlated with clinical course, rejection activity, biopsy results (including genomic analysis), and blood-based measurements including flow cytometric and cytokine analyses, with specific emphasis on humoral immune responses.

Performing Institution: Louisville

Task 1. To establish and maintain a database of imaging data and clinical follow-up including immune monitoring assays.

Task 2. To perform imaging clinical and immune monitoring of subjects as well as historical controls for comparison of rejection episodes, humoral immune status and mature lineage and cytokine analysis of peripheral blood Regulatory review and approval process (months 1-4).

Subtask 2.1. To collect data regarding non-histologic indices of rejection such as hand volume (edema), presence of rash or erythema, and level of involvement, i.e. localized or generalized involving a named (i.e. 25%) percentage of the allograft dorsal or ventral surface.

Subtask 2.1. To perform immune monitoring assays on peripheral blood lymphocytes at rejection and following resolution.

Aim 7. To establish disease mechanisms associated with vasculopathy in pre-clinical models of VCA. Hypothesis: VCA-associated macro- and microvasculopathies are due to chronic and multiple acute rejection activities, and can be exacerbated to confluent aggressive vasculopathy by non-alloimmune triggers. We will perform vascular imaging assessments utilizing mouse preclinical models of VCA in experiments with defined rejection regimens. In addition, we will use vascularized composite autograft models to evaluate the effects of inflammation and antirejection medications in the absence of active rejection. Our evaluations will include molecular and histologic analyses in combination with imaging-based measurements, including those utilizing already developed and tested targeted bioactive contrast agents for use in assessing vascular status.

Performing Institution: Louisville (in collaboration with Penn, Emory and Maryland)

Task 1: To perform osteomyocutaneous (hindlimb) allogeneic VCA in rodents (Regulatory review and approval process.

1. **Task 2:** To establish baseline and experimental imaging standards in rodent model
2. **Subtask 2a:** To transplant groups of animals and follow and image over a 28-90 day period
3. **Subtask 2b:** To perform immunologic and histologic analysis of VCA recipients
4. **Task 3:** To perform murine transplants involving pharmacological and genetic perturbations to allo-rejection
5. **Subtask 3.1:** To transplant groups of animals evaluating experimental interventions with imaging
- 6.

7. **Aim 8– To develop standardization of protocols and clinical monitoring and treatment for VCA targeting vascular health.** We propose to serve as the central site for the standardization of (a) bioimaging assessment of vasculopathies in hand and face allotransplants, and (b) Collaborate with consortium members in submission of biorepository samples and digitization of existing Hematoxylin and Eosin slides of clinical VCA biopsies.
8. **Focus areas:** Clinical Monitoring of Composite Tissue allotransplant recipients, and Established Practice and Protocol
9. **Performing Institution:** All sites
10. **Task 1:** To establish reproducible and HIPAA compliant protocols for UBM, MLDI and SPY imaging in VCA recipients (Regulatory review and approval process (1-4). Data collection
11. **Task 2:** To implement and maintain database and data sharing protocols for clinical and experimental animal data with consortium members
12. **Task 3:** To participate with consortium members in submission of historical and prospective VCA patient histological slides and biopsy samples for digitization using the Aperio system.

What was accomplished under these goals?

In the first year of this grant, we successfully obtained ACURO approval for the rat osteomyocutaneous flap and have started the transplants and imaging studies in the rat model. We were able to recruit Dr. Zheng, who has arrived from China and has completed all of the required regulatory training with respect to human subjects, HIPAA, laboratory safety, animal care and use, as well as research integrity training

We are pleased to report that we have purchased the Novadaq LUNA fluorescence angiography unit (under separate funding), and several of the hand surgeons participating in the hand transplant protocol have attending training sessions using the equipment. In addition, the company Novadaq, has agreed to provide us with an additional unit to perform similar studies in the rat experimental protocol outlined in aim 7 of the proposal. Rob Reed and Dr. Hoying have established the myocutaneous and osteomyocutaneous flap, and Dr. Zheng is working with Dr. Hoying and Williams on establishing the laboratory protocols that will be used to image the rodents after their VCA transplants.

In the first year of the grant have met with representatives of Visual Sonics and have made arrangements to have new software that will reduce the subjectivity of measuring artery and vein wall thickness, especially the arterial wall intima in our hand transplant patients. This software is due to be installed and training will be provided in the first quarter of year 2 of the grant.

In addition to the ongoing monitoring of all of the current hand transplant patients, as

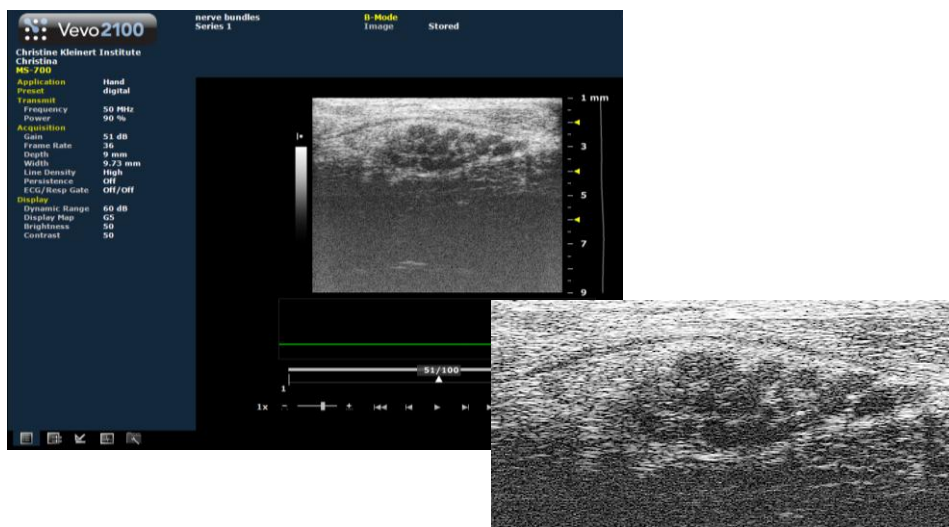


Figure 1: High Resolution Ultrasound imaging of normal Medial nerve using the Vevo 2100. Note the individual nerve bundles within the nerve that can be non-invasively distinguished with respect to size and number

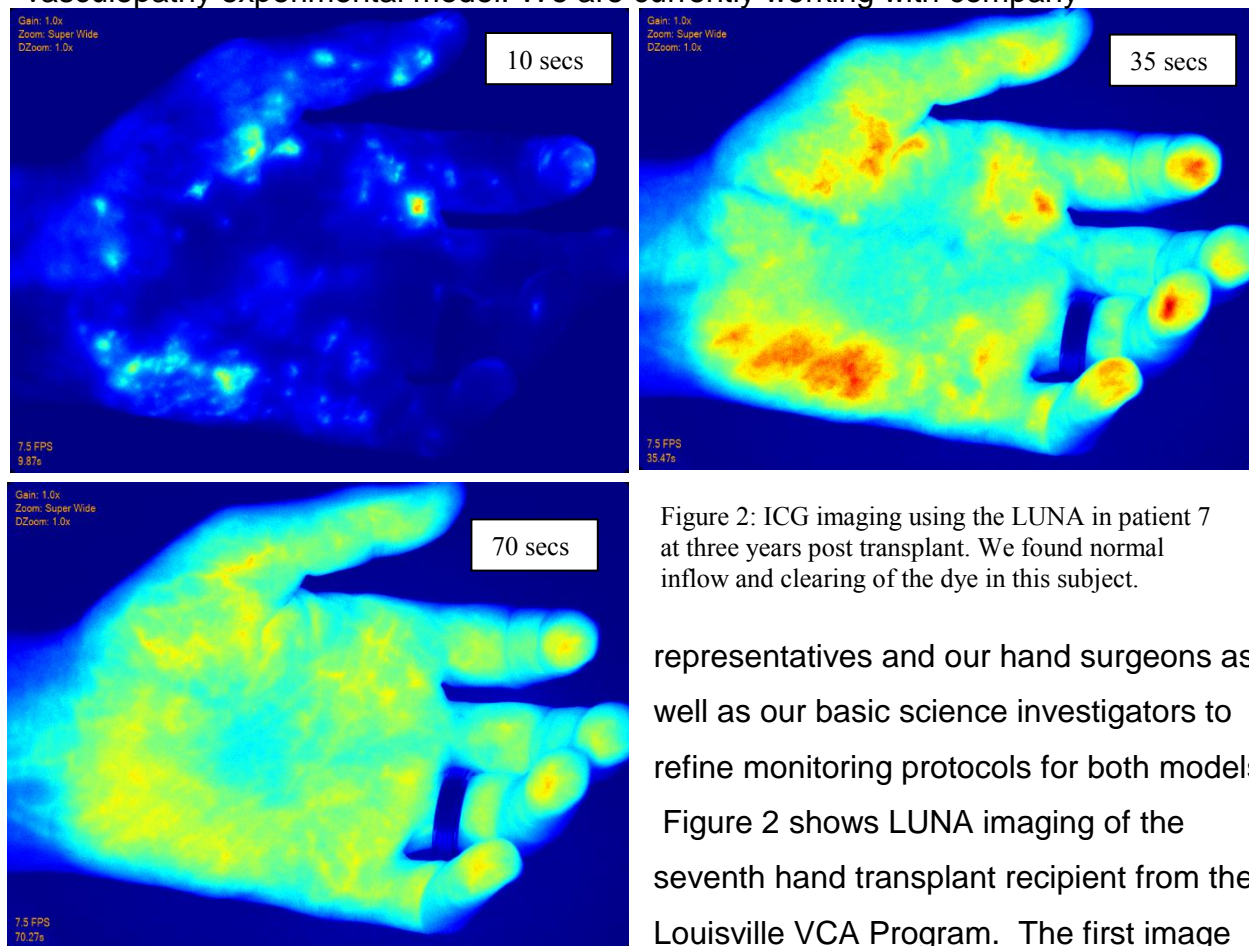
well as
collecting
images on
subject who are
being screened
for transplant,
we have
initiated studies
that will use the
Vevo 2100 to

monitor the
medial and
ulnar nerves.

Using the very high resolution probes we are able to image the nerve bundles within the nerve. With the new software upgrade, we will be better able to quantitate the number and size of the bundles. As the study progresses we hope to be able to correlate changes in function with changes in the images collected. As an off shoot of these studies we are also planning to conduct a study of hand surgery patients who have sustained an injury to the medial or ulnar nerve and see if loss of function correlates to the quality/quantify of nerve bundles that can be viewed with the Vevo 2100. Figure 1 shows an image of a normal median nerve taken with the 70 MHz probe, showing the individual nerve bundles. With this technology we can get near-microscopic images in

a non-invasive manner, and correlate these images with patient clinical course and graft function.

We have obtained a clinical LUNA fluorescence angiography unit and an additional research fluorescence angiography unit (under separate funding) to use in the vasculopathy experimental model. We are currently working with company



representatives and our hand surgeons as well as our basic science investigators to refine monitoring protocols for both models. Figure 2 shows LUNA imaging of the seventh hand transplant recipient from the Louisville VCA Program. The first image shows the transplanted hand about 10 seconds after I.V. infusion of ICG dye in the contralateral native arm. The second and third images are about 35 and 70 seconds later. This technology can quantitate the amount of time required for the vasculature to distribute and then clear the dye.

In addition to the use of the use of the LUNA unit to study vascularity of the transplanted hand, we will also use this technology to image lymphatic drainage of the

hand. We have initiated a study of sub-cutaneous injection of small quantities (less than 100 ul) of the dye and then imaging the injected site over hours and days to follow the clearance of the dye by the lymphatic system in normal controls. This study will be important to establish normal parameters for the assessment of transplanted subjects.

Although outside the funding of the current grant, an important part of our study is our success in enrolling and transplanting VCA recipients. We are putting significant effort into finding and screening potential candidates. To date, the majority of candidates who approach our program have failed our screening procedures. However, those programs with active clinical VCA programs understand how critical the screening process is to achieving good outcomes. Strict adherence to our inclusion and exclusion criteria are paramount to the success of this project as well.

The current working summary of potential and pending candidates for hand transplantation is as follows:

Male age 39, unilateral amputee - denied in July screening committee, medically fit, social support issues

Male age 42, bilateral amputee - referred for BKA due to chronic osteomyelitis in heel, eligible for listing for hand transplant, will wait until rehab of prosthesis for lower limb is complete

Male age 32, unilateral amputee - pending financial review to come to Louisville for medical and psychosocial testing

Male age 67, previously listed for hand transplant, family concerns precluded acceptance, those have been resolved and subject is coming back to Louisville for re-evaluation and potential listing

Female age 51, medically acceptable, financial and psychosocial issues require resolution before subject could be listed. The candidate is working on these issues.

Male age 31, excellent candidate, approved for listing, waiting on workman's comp settlement

Male age 32, excellent candidate, family situation changed, subject still interested in transplant once family issues are more manageable.

Female age 37: Currently listed for bilateral hand transplant, but subject has high PRA

In addition to studies focused on improving and standardizing monitoring of VCA recipients in Aim 6 and 8, Aim 7 will address the hypothesis that VCA-associated macro- and microvasculopathies are due to chronic and multiple acute rejection activities, and can be exacerbated to confluent aggressive vasculopathy by non-alloimmune triggers. We will perform vascular imaging assessments utilizing rodent preclinical models of VCA in experiments with defined rejection regimens. In addition, we are using vascularized composite autograft models to evaluate the effects of inflammation and antirejection medications in the absence of active rejection. The work in this Aim is guided by 3 tasks, the first two of which are relevant to this year 1 progress report.

Task 1: To perform osteomyocutaneous (hindlimb) allogeneic VCA in a rodent model

Task 2: To establish baseline and experimental imaging standards in rat model

Task 3: To perform rat transplants involving perturbations to allo-rejection

Within the months 1-12 of the project, we have: 1) obtained ACURO approval for a rat model of VCA rejection, 2) developed the rat model of VCA rejection, 3) established baseline imaging standards for the progression VCA regression in the model, 3) established flow cytometry standards for assessing immune cell population in the model, 4) established histology scoring standards for the progression VCA regression in the model.

Task 1: To perform osteomyocutaneous (hindlimb) allogeneic VCA in rat.

We originally proposed to utilize a mouse model of VCA in our studies. However, for practical and logistical reasons, we focused our attention on developing a rat model of VCA. In developing the model, we focused several key issues related to the goals of this Aim and of the consortium overall. First, it was important that we include bone (with marrow intact) and skin in the graft. Second, it was not necessary for our purposes that

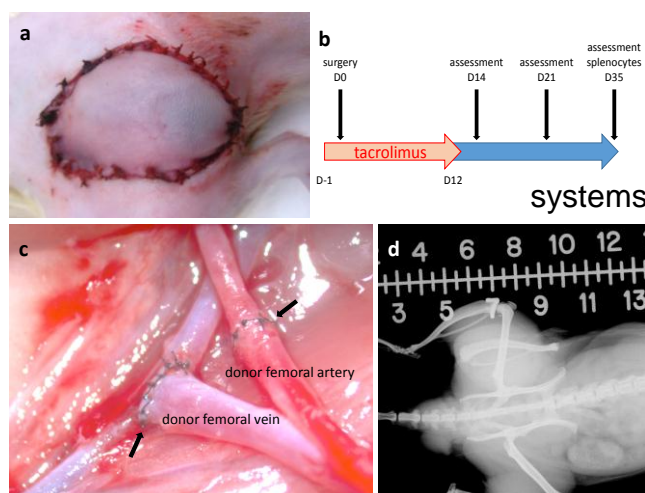


Figure 3. a) Gross image of complete graft transplant in inguinal pocket of recipient. b) Experimental protocol. c) Completed anastomoses. d) X-ray of indicating the orientation of the graft.

the graft was functional, eliminating the need to reinnervate the graft. Third, the graft needed to be accessible to imaging

systems. Finally, for through-put reasons, the

grafting surgeries needed to be readily performed, which is easier to do in the larger rat model. With these considerations in mind, we developed a new model of rat VCA in which the distal hindlimb (between the knee and the ankle) of a donor (BN), including the overlying skin, was transplanted into the

inguinal position on the recipient (Lewis) with the vascular supply to the graft occurring via femoral artery and vein anastomoses (**Figure 3**). The IACUC approved protocol was approved by ACURO in May 2014.

In preparation of the graft, a vascular leash containing both the femoral artery/vein pair and distal iliac artery/vein regions was isolated. Furthermore, the musculature of the lower hindlimb was resected to leave only the gastrocnemius remaining, the primary

muscle group supported by the isolated vascular leash. Care was taken in preparing the graft to preserve artery perforators supporting skin perfusion. The graft is transplanted in the inguinal pocket of the recipient with the distal end of the

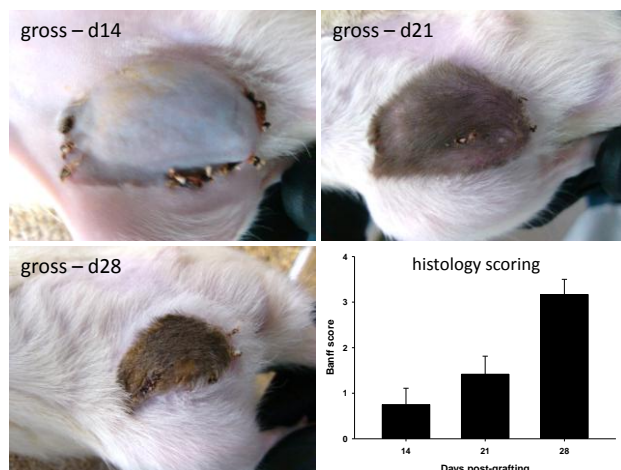


Figure 4. Gross images and histology rejection scoring of grafts over the course of graft rejection. Immune suppression was withdrawn at day 12.

tibia/fibula pointing anterior (**Figure 3**). The femoral artery of the donor was attached to the femoral artery of the recipient via an end-end anastomosis. While the vein anastomosis involved an end (donor)-side (recipient) arrangement (**Figure 3**).

Task 2: To establish baseline and experimental imaging standards in rat VCA model. Because the goal is to evaluate vasculopathies in VCA, including the consequences of rejection on vascular integrity, we employed an initial immune-suppression protocol designed to provide baseline information of vascular function during graft healing without rejection, vascular function post-healing without rejection, and vascular function with rejection. Therefore, our first-pass immune suppression regimen involved placing the recipient on tacrolimus for 12 days followed by complete withdrawal of the immune suppressant. Assessment of graft health occurred during this entire time course.

With the rat VCA model established, we implemented a broad regimen of assessments involving gross examination, biopsies, blood draws, and imaging of vascular performance intended to characterize graft health and formalize imaging procedures. We now have a well-defined time-course of graft progression with early signs of rejection occurring approximately 1 week after withdraw of tacrolimus (day 14 in our protocol) and frank rejection by 3 weeks (day 28) (**Figure 4**). The proposed work for this task also involved the development of protocols for implementing two new imaging modalities: IR-ICG imaging (microvascular) and high-resolution ultrasound (macro-vascular). We are currently exploring the utility of infra-red imaging of an i.v. injected

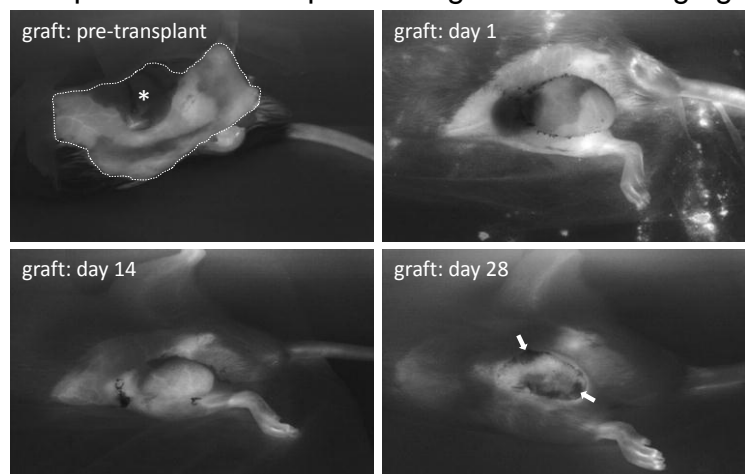


Figure 5. IR-ICG mapping of microvascular perfusion in the graft. In the pre-transplant panel where the graft is still attached to the donor circulation, the dashed outline shows the overlying skin of the graft and the asterisk indicates a region of poor perfusion (this region is removed at the time of transplant). Arrows in the day 28 image indicate dark regions of poor perfusion.

fluorescent dye, indocyanine green (ICG) as a means to visualize zones of limited perfusion as a complement or substitute for Doppler imaging. IR-ICG imaging is commonly used clinically by plastic surgeons for mapping hypo-perfused zones in reconstructive tissue flaps. Using IR-ICG imaging indicates that blood flow dynamics within the graft mirrors the rejection course with high perfusion correlating with low rejection status and vice versa (**Figure 5**). Finally, as a means to assess immune status, we have developed a flow cytometry analytical panel for determining the lymphocyte profile in splenocytes harvested at the time of explant. This panel enables us to examine a broad distribution of lymphocyte types, including FoxP3⁺ regulatory T-cells. As expected, these immune-suppressive T_{regs} are proportionally reduced during frank rejection (**Figure 6**).

Currently, we are preparing a manuscript to describe the VCA model and our present findings. During the next project period, we will initiate the experiments of *Task 3* involving different immune-suppression regimens, as described in the grant application, to begin understanding the impact these drugs have on graft vascular health. As part of

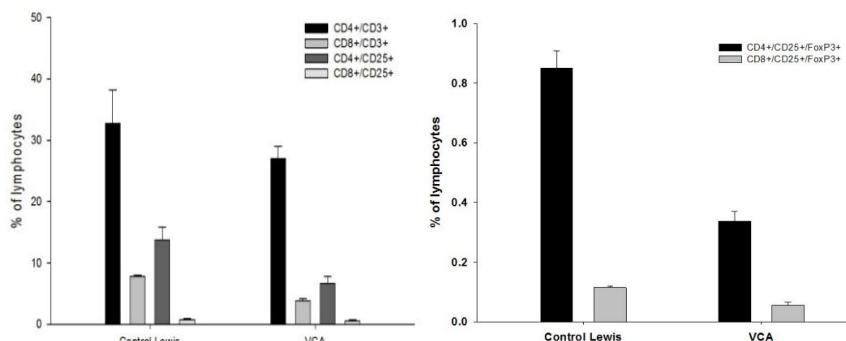


Figure 6. Flow cytometry of splenocytes harvested at day 28, a time of frank rejection in the graft.

this, we will continue to evaluate IR-ICG imaging as a means to assess microvascular performance during grafting. This includes developing the algorithms to

quantify perfusion within the graft from these qualitative images. Also, we will initiate the use of high-resolution ultrasound in our experiments to assess conduit vessel status during graft progression.

What opportunities for training and professional development has the project provided?

The hand surgeons involved in the clinical trial of hand transplantation received training in the use of the LUNA fluorescence angiography unit.

How were the results disseminated to communities of interest?

We have had abstracts accepted to local, national and international meetings including the Tri-state Hand Surgery meeting in Cincinnati, OH, the World Transplant Congress in San Francisco, and the American Society of Reconstructive Surgery to be held in Chicago in November of this year.

What do you plan to do during the next reporting period to accomplish the goals?

Currently, we are preparing a manuscript to describe the rodent VCA model and our present findings. During the next project period, we will initiate the experiments of *Task 3* involving different immune-suppression regimens, as described in the grant application, to begin understanding the impact these drugs have on graft vascular health. As part of this, we will continue to evaluate IR-ICG imaging as a means to assess microvascular performance during grafting. This includes developing the algorithms to quantify perfusion within the graft from these qualitative images.

In the next reporting period we will also focus on refining the techniques for monitoring vascular health in our hand transplant patients as well as potentially monitoring nerve recovery and function using the Vevo 2100, including the new software and updates for objectively measuring structure size and volume in our images. We will also design and obtain approval for studies using the LUNA fluorescence angiography using to monitor lymphatic drainage in our hand transplant patients. As we initiated studies it became clear that additional knowledge is required regarding the clearing of dye by the lymphatics in normal controls. These studies will be critical to the standardization and interpretation of imaging studies and monitoring in VCA recipients.

As the collaborating centers come on line with clinical studies we will submit an IRB protocol that will cover collection of data from centers other than Louisville, as well as for our own patients that will allow us to share biopsy specimens and clinical data with our collaborators.

IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Our initial studies in monitoring subjects using IR-ICG techniques (using the LUNA fluorescence angiography unit) suggest that there may be a distinct difference in how the lymphatics drain in transplant recipients vs. normal controls. If we can define these differences, and determine a way to normalize or optimize drainage in transplant recipients, we expect that functional outcomes will be improved. Additionally the ability to monitor nerve function by an anatomic measurement (counting the nerve bundles) may be an important tool to gauge progress in these patients. The availability of the rodent model will allow us to test the effect of different interventions and stages of rejection on these monitoring techniques.

What was the impact on other disciplines?

While the target population of this proposal is VCA recipients, we expect that significantly larger patient populations will also benefit. Cancer patients, especially breast cancer patients will benefit from a better understanding of lymphatic drainage in the upper extremity. In addition, thousands of patients a year have traumatic severing of the digital, medial and ulnar nerves. A technique to monitor recovery would be very helpful in testing interventions to improve nerve recovery in these patients as well.

What was the impact on technology transfer?

These studies have the potential to improve utilization of both fluorescence angiography and high resolution ultrasound through novel applications to understand

vessel perfusion, lymphatic drainage and recovery of nerve bundles in ligated and repaired peripheral nerves.

What was the impact on society beyond science and technology?

The goal of this proposal is to improve the quality of life of persons who receive a VCA transplant for the treatment of catastrophic tissue loss. While we are striving to measure, improve and standardize this treatment modality, the ultimate judgment of whether the lives of these patients are restored are made by the patients and their families. If we can play some role in restoring the limbs or face of a soldier to as “normal” as possible, and allow them the best opportunity to integrate back in society, our goal will be achieved.

CHANGES/PROBLEMS:

Changes in approach and reasons for change.

The only change in approach was to switch from a mouse model to a rat model for our VCA rodent model. This change was undertaken for technical reasons, and to have vessels and structures that are easier to image with our equipment. This request was submitted to and approved by ACURO. We still plan to pursue the mouse model to address specific mechanistic questions that may arise as the grant progresses, and as data is generated by our colleagues at the University of Pennsylvania.

Actual or anticipated problems or delays and actions or plans to resolve them

The major delay in these studies will be the accrual of VCA recipients. We cannot control the number of patients transplanted. In our clinical trial of hand transplantation (funded outside the current grant) we are aggressively screening candidates and listing them for transplantation as they are approved. We have a patient who has been listed for hand transplantation for over a year, for whom we have not been able to find a donor because of preformed antibodies. We are hopeful that the recent implementation of UNOS oversight, and the ability to list this patient nationally will

increase her chances of finding a donor. With the additional patients we plan to list, we are confident we will have additional VCA recipients to monitor.

Changes that had a significant impact on expenditures

The most difficult personnel to hire on this grant was the post doctoral fellow who has experience in microsurgery and immunologic techniques, as well as computer skills. Dr. Zheng was not hired until May and this impacted our spending on personnel for the first year of the grant.

Significant changes in use or care of human subjects – None to report

Significant changes in use or care of vertebrate animals. – None to report other than the use of the rat VCA model which was approved by ACURO.

Significant changes in use of biohazards and/or select agents – N/A

PRODUCTS:

"Nothing to Report."

Publications, conference papers, and presentations

"Incidence of successful steroid weaning in a series of eight hand transplant recipients" C.L. Kaufman, R. Ouseph, J.E. Kutz, H.Y. Tien, Y. Manon-Matos, B. Blair, and M.R. Marvin. Christine M. Kleinert Institute, Transplant Center, Jewish Hospital, University of Louisville and the Kleinert Kutz Hand Care Center, Louisville, KY, has been accepted for podium presentation at the upcoming American Society for Reconstructive Transplantation 4th Biennial Meeting, November 20-22, 2014, at the Drake Hotel in Chicago, Illinois.

Website(s) or other Internet site(s) – None to report

Technologies or techniques – None to report

Inventions, patent applications, and/or licenses – None to report

Other Products – None to report

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

<i>Name:</i>	Christina Kaufman PhD
<i>Project Role:</i>	Primary Investigator
<i>Researcher Identifier (e.g. ORCID ID):</i>	
<i>Nearest person month worked:</i>	12 months @ 10% effort
<i>Contribution to Project:</i>	Dr. Kaufman has met on a consistent basis with local grant co-investigators and initiated studies on the LUNA IR/ICG unit as well as the Vevo 2100. She also oversees the day to day administration of the grant and the hand transplant protocol with the Louisville VCA Program.
<i>Name:</i>	Jay Hoying PhD
<i>Project Role:</i>	Co-Investigator
<i>Researcher Identifier (e.g. ORCID ID):</i>	
<i>Nearest person month worked:</i>	12 months @ 8% effort
<i>Contribution to Project:</i>	Dr. Hoying has met on a consistent basis with local grant co-investigators and obtained approval for the IACUC protocol through the U of L IRB. Dr. Hoying also initiated discussions with the JH/CHI IT department. Dr. Hoying also works with Rob Reed in performing the rat VCA flaps, and the imaging studies in the experimental model.

<i>Name:</i>	Joseph E. Kutz MD
<i>Project Role:</i>	Co-Investigator
<i>Researcher Identifier (e.g. ORCID ID):</i>	
<i>Nearest person month worked:</i>	12 months @ 5% effort
<i>Contribution to Project:</i>	Dr. Kutz has met on a consistent basis with local grant co-investigators to discuss details of the clinical monitoring protocols.
<i>Name:</i>	Michael R. Marvin MD
<i>Project Role:</i>	Co-Investigator
<i>Researcher Identifier (e.g. ORCID ID):</i>	
<i>Nearest person month worked:</i>	12 months @ 2% effort
<i>Contribution to Project:</i>	Dr. Marvin has met on a consistent basis with local grant co-investigators to discuss details of the clinical monitoring protocols.
<i>Name:</i>	Stuart K. Williams PhD
<i>Project Role:</i>	Co-Investigator
<i>Researcher Identifier (e.g. ORCID ID):</i>	
<i>Nearest person month worked:</i>	12 months at 8% effort
<i>Contribution to Project:</i>	Dr. Williams has met on a consistent basis with local grant co-investigators to discuss details of the clinical monitoring protocols as well as the IACUC protocols and the imaging studies in the experimental model.
<i>Name:</i>	Brenda Blair
<i>Project Role:</i>	Research Nurse
<i>Researcher Identifier (e.g. ORCID ID):</i>	
<i>Nearest person month worked:</i>	12 months at 20% effort
<i>Contribution to Project:</i>	Ms. Blair has been working on establishing protocols and methods for IRB and working with Drs. Kaufman, Kutz and Marvin on protocols and patient follow up.
<i>Name:</i>	Lei Zheng, MD, PhD
<i>Project Role:</i>	Post doctoral fellow
<i>Researcher Identifier (e.g. ORCID ID):</i>	
<i>Nearest person month worked:</i>	5 months at 100% effort

Contribution to Project:

Dr. Zheng has completed the regulatory training necessary to participate in animal experiments and IRB protocols. He has observed animal VCA flap procedures (performed under separate funding) and is participating in drafting protocols for in vitro assays and archiving of samples. He is also participating in the standardization of imaging monitoring protocols.

Name:

Robert Reed

Project Role:

Technician

Researcher Identifier (e.g. ORCID ID):

Nearest person month worked:

12 months at 30% effort

Contribution to Project:

Mr. Reed has been working on establishing protocols and methods for IACUC project and working with Drs. Hoying and Williams on preparation of protocols. He has established and mastered the microsurgical techniques of the rat VCA model with Dr. Hoying.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

"Nothing to Report."

What other organizations were involved as partners?

Provide the following information for each partnership:

Organization Name: Jewish Hospital Foundation (JHF) and Jewish Hospital (Part of KentuckyOne Health)

Location of Organization: Louisville, KY

Partner's contribution to the project – JHF and JH have provided \$1.5 million in funding to cover cost of screening, transplanting and patient follow up for hand transplant recipients that are not covered by insurance.

Organization Name: Kleinert Kutz Hand Care Center

Location of Organization: Louisville, KY

Partner's contribution to the project – The Kleinert Kutz Hand Care Center supplies all of the surgeons which perform the actual hand transplants and help to follow the patients post transplant. In addition, KKHCC staff also participate in the screening of potential hand transplant candidates. The surgeons do not charge for these efforts.

SPECIAL REPORTING REQUIREMENTS – None to report

APPENDICES – None to report